FILE 'CAPLUS' ENTERED AT 15:21:47 ON 16 JAN 2003
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FILE COVERS 1907 - 16 Jan 2003 VOL 138 ISS 3
FILE LAST UPDATED: 15 Jan 2003 (20030115/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 1 L3

=> d bib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2002:575064 CAPLUS
DN 137:125091
TI Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related compounds, and compositions thereof as TNF-.alpha. inhibitors for treatment of cancer, inflammatory disorders, heart disease, and related disorders
IN Robarge, Michael J.; Chen, Roger Shen-Chu; Muller, George W.; Man, Hon-Wah
PA Celgene Corporation, USA
SO PCT Int. Appl., 224 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002059106	A1	20020801	WO 2001-US50401	20011221
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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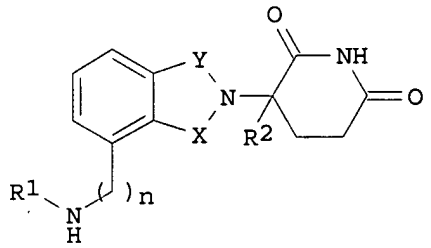
PRAI	US 2000-258372P	P	20001227		
	US 2001-972487	A	20011005		

OS MARPAT 137:125091
GI



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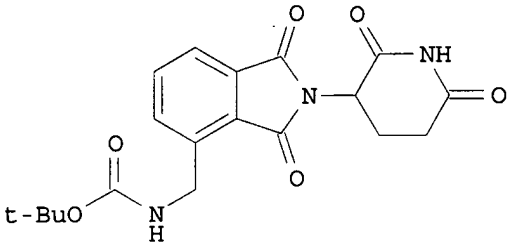

II

AB Title isoindole-imides I [wherein one of X and Y is CO and the other is CH2 or CO; R1 = H, (cyclo)alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, COR3, CSR3, CO2R4, alkyl-(NR6)2, alkyl-OR5, alkyl-CO2R5, CONHR3, CSNHR3, CON(R3)2, CSN(R3)2, or alkyl-OCOR5; R2 = H, benzyl, alkyl, alkenyl, or alkynyl; R3 = independently (cyclo)alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, alkyl-N(R6)2, alkyl-OR5, alkyl-CO2R5, alkyl-OCOR5, or CO2R5; R4 = alkyl, alkenyl, alkynyl, alkyl-OR5, benzyl, aryl, alkylheterocycloalkyl, or alkylheteroaryl; R5 = alkyl, alkenyl, alkynyl, benzyl, aryl, or heteroaryl; R6 = independently H, alkyl, alkenyl, alkynyl, benzyl, (hetero)aryl, or alkyl-CO2R5; or R6 groups may join to form a heterocycloalkyl group; n = 0-1; with the proviso that when n = 0, R1 .noteq. H; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, enantiomers, diastereomers, racemates, or mixts. of stereoisomers thereof] were prepd. for reducing the level of cytokines and their precursors in mammals. In particular, the invention pertains to isoindole-imide compds. that are potent inhibitors of the prodn. of TNF-.alpha. (no data). For example, Me 2-(methoxycarbonyl)-3-nitrobenzoate was hydrogenated with 10% Pd/C (87%). The amine was converted to the nitrile by diazonium salt formation effected by treatment with NaNO3 followed by cyanide formation using classic Sandmeyer procedure (65%). The nitrile was reduced with 10% Pd/C in MeOH and aq. HCl under hydrogen to afford Me 3-aminomethyl-2-(methoxycarbonyl)benzoate.bul.HCl (90%), which was treated with TEA and then reacted with di-t-Bu dicarbonate to give the carbamate (93%). Cyclization with 3-aminoglutarimide.bul.HCl using diisopropylethylamine in DMF produced II (82%). The 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones and pharmaceutical compns. comprising them are useful for treating or preventing diseases or disorders in mammals, e.g. cancers, such as solid tumors and blood-born tumors; heart disease, such as congestive heart failure; osteoporosis; and genetic, inflammatory, allergic, and autoimmune diseases (no data).

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1                STR
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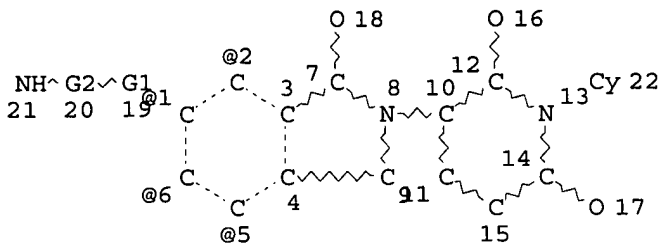


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE


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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          656 TO     1544
PROJECTED ANSWERS:               3 TO      163

L2            3 SEA SSS SAM L1

=> d scan

L2   3 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN   4-Pyridinecarboxamide, N-[[2-(2,6-dioxo-3-piperidinyl)-2,3-dihydro-1,3-
     dioxo-1H-isoindol-4-yl]methyl]- (9CI)
MF   C20 H16 N4 O5
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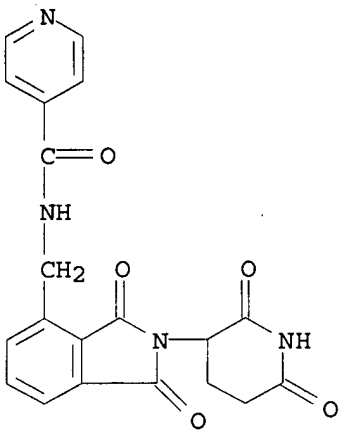

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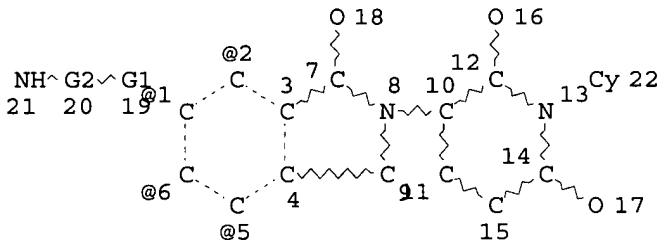

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

=> s l1 ful
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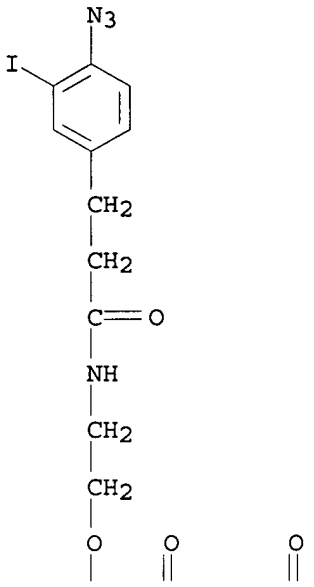
SEARCH TIME: 00.00.01

L3 75 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 150.95 151.16

AN 1996:450807 CAPLUS
DN 125:158041
TI Binding of thalidomide to .alpha.1-acid glycoprotein may be involved in its inhibition of tumor necrosis factor .alpha. production
AU Turk, Benjamin E.; Jiang, Hongsi; Liu, Jun O.
CS Center Cancer Research, Department Biology Chemistry, Massachusetts Institute Technology, Cambridge, MA, 02139, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(15), 7552-7556
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB In addn. to its well known sedative and teratogenic effects, thalidomide also possesses potent immunomodulatory and antiinflammatory activities, being most effective against leprosy and chronic graft-vs.-host disease. The immunomodulatory activity of thalidomide has been ascribed to the selective inhibition of tumor necrosis factor .alpha. from monocytes. The mol. mechanism for the immunomodulatory effect of thalidomide remains unknown. To elucidate this mechanism, we synthesized an active photoaffinity label of thalidomide as a probe to identify the mol. target of the drug. Using the probe, we specifically labeled a pair of proteins of 43-45 kDa with high acidity from bovine thymus ext. Purifn. of these proteins and partial peptide sequence detn. revealed them to be .alpha.1-acid glycoprotein (AGP). We show that the binding of thalidomide photoaffinity label to authentic human AGP is competed with both thalidomide and the nonradioactive photoaffinity label at concns. comparable to those required for inhibition of prodn. of tumor necrosis factor .alpha. from human monocytes, suggesting that AGP may be involved in the immunomodulatory activity of thalidomide.
IT **390367-55-2P 390367-61-0P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(binding of thalidomide to .alpha.1-acid glycoprotein may be involved in its inhibition of tumor necrosis factor .alpha. prodn.)
RN 390367-55-2 CAPLUS
CN Benzenepropanamide, 4-azido-N-[2-[[2-(2,6-dioxo-3-piperidinyl)-2,3-dihydro-1,3-dioxo-1H-isoindol-4-yl]oxy]ethyl]-3-iodo- (9CI) (CA INDEX NAME)

PAGE 1-A



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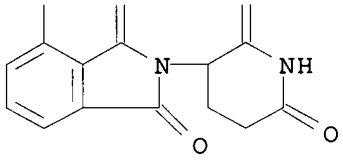

RN 390367-61-0 CAPLUS

CN Benzenepropanamide, 4-azido-N-[2-[[2-(2,6-dioxo-3-piperidinyl)-2,3-dihydro-1,3-dioxo-1H-isoindol-4-yl]oxy]ethyl]-3-(iodo-125I)- (9CI) (CA INDEX NAME)

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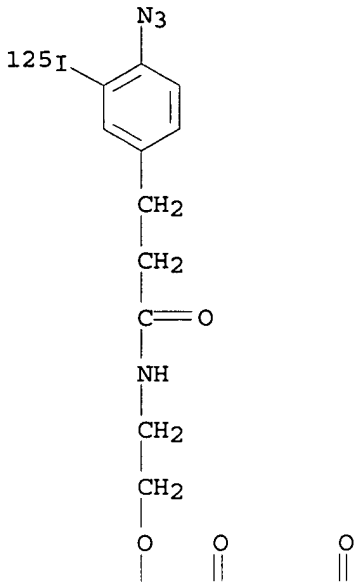

PAGE 2-A